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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/990,456	11/14/2001	Avi J. Ashkenazi	P2730P1C22	4092

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EXAMINER	
JIANG, DONG	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 06/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/990,456	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/14/01*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *119-124* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *119-124* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/24/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED OFFICE ACTION

Applicant's preliminary amendment filed on 14 November 2001 is acknowledged and entered. Following the amendment, the original claims 1-118 are canceled, and the new claims 119-124 are added.

Currently, claims 119-124 are pending and under consideration.

Formal Matters:

Priority

This application claims priority to US provisional application 60/088,810, PCT/US99/12252, 60/141,037, 09/380,137, PCT/US00/08439, and US application 09/941,992. For the following reasons, the Examiner finds that the present claims 119-131 are not supported in the manner required by 35 U.S.C. 101 and 112, first paragraph by the first four prior applications, thus none of present claims is entitled to the benefit of the filling date of those prior applications.

The priority documents 60/088,810, PCT/US99/12252, 60/141,037, 09/380,137 merely disclose a polypeptide having SEQ ID NO:285, which is designated PRO7170, and they fail to provide any specific, substantial utility, nor guidance or working examples to teach how to used the claimed invention. Therefore, the Examiner is not able to establish that the priority documents 60/088,810, PCT/US99/12252, 60/141,037, 09/380,137 satisfy the utility/enablement requirement of 35 U.S.C. 101/112, first paragraph. As such, the claims of the instant application are not entitled to the benefit of the filling date of these prior applications. Priority is granted to the filing date of the later application, PCT/US00/08439, filed on 30 March 2000, wherein some specific and substantial biological properties of said PRO7170 polypeptide were disclosed, such as inducing re-differentiation of chondrocytes (Example 159).

Title

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the elected claims are directed.

Objections and Rejections under 35 U.S.C. §101 and §112:

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 119 and 124 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claim 119, as written, does not sufficiently distinguish over antibodies as they exist naturally because the claim does not particularly point out any non-naturally occurring differences between the claimed product and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See *Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "isolated" or "purified". See MPEP 2105.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 122 and 124 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 122 is indefinite for the recitation of "the antibody ... is an antibody fragment" as an antibody cannot be an antibody fragment in the same time.

Claim 124 is indefinite for the recitation of "specifically binds" because it is not defined in the specification; one of skill in the art would not know what the metes and bounds of "specifically" were intended to be and would not know what level of binding, and thus what antibodies, were included in the limitations of the claims. Further, it is unclear how the term "specifically binds" differs from "binds" in claim 124.

Rejections Over Prior Art:

The following rejections under 35 U.S.C. § 102 and 103 are made in view of the determination that the effective filing date for the instantly claimed invention is 30 March 2000, which is the filing date of the application of PCT/US00/08439.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 119, 120 and 124 are rejected under 35 U.S.C. 102(a) as being anticipated by Jacobs et al., US5,965,397.

Jacobs discloses a human secreted protein having an amino acid sequence of SEQ ID NO:19, which comprises amino acids 1-337 of the present SEQ ID NO:285 with 99.4% sequence identity (see computer printout of the search results). Additionally, Jacobs teaches an antibody binding to said polypeptide or a fragment thereof, including monoclonal antibody, and its potential use in diagnosis and treatment (the paragraph bridging columns 41 and 42). The reference, therefore, anticipates the present claims 119, 120 and 124.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claim 121 is rejected under 35 U.S.C. 103(a) as being unpatentable over Jacobs et al., US5,965,397, as applied to claims 119, 120 and 124 above, and further in view of Riechmann et al. (Nature, 1988, 332:323-327).

The teachings of Jacobs are reviewed above. Jacobs does not specifically teach a humanized antibody.

Riechmann teaches a strategy to make a humanized antibody (see page 325-327 of the reference). A humanized antibody allows an antibody generated from a non-human origin to retain the specificity and biological effects of the original antibody but have the potential to be nonimmunogenic in humans. The effector functions of such a chimaeric antibody can be selected or tailored. Additionally, the use of human isotypes minimize the anti-globulin response during therapy by avoiding anti-idiotypic antibodies (see page 323 of the reference).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the antibody disclosed by Jacobs to a humanized antibody following the teachings by Riechmann. The person of ordinary skill in the art would have been motivated to make such a modification for therapeutic uses to neutralize the protein, such as treating conditions associated with the protein and some forms of cancer with abnormal expression of the protein, as suggested by Jacobs (column 41, lines 63-67), and to obtain the known and expected advantages taught by Riechmann, and reasonably would have expected success because Riechmann has demonstrated such antibody.

Claim 122 is rejected under 35 U.S.C. 103(a) as being unpatentable over Jacobs et al., US5,965,397, as applied to claims 119, 120 and 124 above, and further in view of Sandhu (Critical Reviews in Biotech., 1992, 12(5/6): 437-462, especially pages 449-450).

The teachings of Jacobs are reviewed above. Jacobs does not specifically teach an antibody fragment.

Sandhu teaches Fab and Fv fragments of an antibody, and indicates that small antibody fragments, such as Fv, may have important applications in the diagnosis and treatment of tumors, where their small size may allow greater penetration, and are ideal for structural

studies and in vivo imaging (page 449, the last paragraph of the right column), and that single chain Fv fragments have the main advantages of their rapid clearance from human circulation and reduced toxic side effects (page 450, F).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the antibody disclosed by Jacobs to make antibody fragments following the teachings by Sandhu. The person of ordinary skill in the art would have been motivated to make such a modification for the purpose of diagnosis such as detecting the metastatic spread of cancer cells mediated by the protein, as taught by Jacobs (column 42, lines 1-4), and for the advantages in diagnosis with antibody fragments as suggested by Sandhu, and reasonably would have expected success because Sandhu has demonstrated such antibody fragments.

Claim 123 is rejected under 35 U.S.C. 103(a) as being unpatentable over Jacobs et al., US5,965,397, as applied to claims 119, 120 and 124 above, and further in view of Hermanus et al., US 3,654,090.

The teachings of Jacobs are reviewed above. Further, Jacobs teaches that monoclonal antibodies binding to the protein may be useful diagnostic agents for the immunodetection of the protein (column 41, lines 60-63). The primary reference does not specifically teach a labeled monoclonal antibody.

Hermanus teaches a method of making enzyme-labeled antibodies or antigens for the determination of antibodies or antigens. Additionally, the reference teaches that enzymes can be detected in very small amounts; the method avoids the use of radio-isotope techniques, does not requires a radio-isotope equipment, and can be performed in every laboratory; and measuring enzyme activity is usually less time-consuming than counting radio activity (the paragraph bridging columns 1 and 2).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to enzyme-label the antibody taught by Jacobs using the method taught by Hermanus. The person of ordinary skill in the art would have been motivated to do so for the immunodetection of the protein for the purpose of diagnosis because of the advantages

suggested by Hermanus, and reasonably would have expected success because Hermanus has demonstrated that such enzyme-labeled antibody can be used for detection of the specific antigen (Example 5).

Conclusion:

No claim is allowed.

Advisory Information:

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 571-272-0872. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on 571-272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER

Dong Jiang, Ph.D.
Patent Examiner
AU1646
6/21/04